# Applying DTI white matter orientations to finite element head models to examine diffuse TBI under high rotational accelerations

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## Abstract

The in-vivo mechanical response of neural tissue during impact loading of the head is simulated using geometrically accurate finite element (FE) head models. However current FE models do not account for the anisotropic elastic material behaviour of brain tissue. In soft biological tissue, there is a correlation between internal microscopic structure and macroscopic mechanical properties. Therefore, constitutive equations are important for the numerical analysis of the soft biological tissues. By exploiting diffusion tensor techniques the anisotropic orientation of neural tissue is incorporated into a non-linear viscoelastic material model for brain tissue and implemented in an explicit FE analysis. The viscoelastic material parameters are derived from published data and the viscoelastic model is used to describe the mechanical response of brain tissue. The model is formulated in terms of a large strain viscoelastic framework and considers non-linear viscous deformations in combination with non-linear elastic behaviour. The constitutive model was applied in the University College Dublin brain trauma model (UCDBTM) (i.e. three-dimensional finite element head model) to predict the mechanical response of the intra-cranial contents due to rotational injury.

*Key words:* Nonlinear elasticity, Anisotropy, Impact biomechanics, Traumatic brain injury

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### 1 1. Introduction

Nearly two million traumatic brain injuries (TBIs) occur annually in the 2 United States and it is the leading cause of death and disability in 15-24 year-3 olds (Langlois et al., 2004, Sorenson and Kraus, 1991). TBI also accounts 4 for one million hospital admissions annually in the European Union (Bowen 5 et al., 1997). The past two decades have seen a large increase in the use 6 of computational biomechanical models as investigative tools in head injury 7 research (Johnson and Young, 2005; Muller and Ruegsegger, 1995; Ruan et 8 al., 1991, 1994, 1993; Kleiven, 2002; Kleiven and Holst, 2002; Horgan and 9 Gilchrist, 2003, 2004; Miller and Chinzei, 1997). These models use either 10 finite element methods or multi-body dynamic simulations to suggest the 11 tolerance levels for the occurrence of head injury using various measured 12 mechanical parameters and the probability of specific head injury sequelae 13 that are associated with TBI (Auer et al., 2001; Doorly and Gilchrist, 2006; 14 Baumgartner et al., 2001; Willinger and Baumgartner, 2003). 15

Diffuse white matter damage is associated with a large fraction of those 16 patients with poor neurological outcome in adult and paediatric survivors of 17 brain injury, ranging from subtle behavioural changes to significant neurolog-18 ical deficits (Colgan et al., 2010). Biomechanical analyses of high rotational 19 acceleration/deceleration associated with diffuse axonal injury (DAI) sug-20 gest a link between brain material response (strain) and the orientation of 21 the associated injured white matter (Halabieh and Wan, 2008; Parizel et al., 22 1998). 23

Neuronal/axonal injury has been implicated as the leading pathologic 24 lesion of TBI, with secondary damage resulting from numerous neurode-25 generative cascades (Smith and Meaney, 2000). Traumatic axonal injury, 26 attributed to shear and tensile stresses, typically occurs in the white matter 27 of the cerebral hemispheres, corpus callosum, and brain stem, especially in 28 severe TBI (Hurley et al., 2004). Diffuse axonal injury, associated with high 29 rotational acceleration/deceleration, often results in apoptosis at sites distal 30 to the centre of rotation of the head (Conti et al., 1998; Holmin et al., 1998; 31 Williams et al., 2006). 32

Based on the involvement of complex neurocognitive pathways of varying orientations, we hypothesise that the predicted severity and location of the sites of injury are influenced by the orientation of the neuronal fibres in the reference frame of the applied global forces in the FE simulation. The objective of this study is to establish the orientation of the neural fibres within the brain using diffusion tensor imaging and apply these orientations
into the 3D UCDBTM FE model (Horgan and Gilchrist, 2003, 2004) to assess
the effects of anisotropy on simulated results of a high rotational TBI.

## **4** 2. Materials and methods

The method used to define the orientation of the fibres within the brain is magnet resonance diffusion tensor imaging (DTI). Diffusion Tensor Imaging (Basser et al., 1994) is an MRI technique that measures the diffusion orientation of water in tissue. Using the measured diffusion of water within highly directional tissue, for example neuronal white matter, it is possible to extract information relating to the trajectory of axonal fibres within the brain. DTI essentially provides two distinct sets of information based on the Brownian motion of water in the specific tissue being scanned;

13 1. anisotropy of the diffusion (e.g. fractional anisotropy (FA))

<sup>14</sup> 2. direction in which the diffusion is occurring

By assuming that the largest principal axis of the diffusion tensor aligns with the predominant fibre orientation in an MRI voxel, we can obtain 2D or 3D vector fields that represent the fibre orientation at each voxel. The 3D reconstruction of tract trajectories, or tractography, is a natural extension of such vector fields. This is the simplest method of tract generation and is used in this current study, however this method can be prone to error.

The normalised DTI volume used is an example file from Fiber Viewer 21 (Goodlett et al., 2005). The image set voxel size of 2x2x2 mm isotropic and 22 the averaged diffusion vector of the water molecules contained in each voxel 23 is based on six principal diffusion direction gradients. The voxel size is small 24 enough to distinguish white and grey matter (Figure 1 A). The white matter 25 consists of tracts that run along various directions and are large enough to 26 discern visually (Figure 1 A and B). The image resolution is sufficiently high 27 for the white matter tracts to span several voxels. The white matter tracts, 28 in turn, consist of densely packed axons (neuronal projections) in addition 29 to various types of neuroglia and other small populations of cells. Inside 30 the voxel, water molecules are distributed between these cell types and the 31 extracellular space (80-85%) are intracellular). Assuming that the orientation 32 of the largest component of the diffusion tensor represents the orientation of 33 dominant axonal tracts, DTI can provide a 3D vector field, in which each 34 vector represents the fibre orientation denoted by  $\lambda$  (Figure 1 C and Figure 35



2). Currently, there are several different approaches to reconstruct white

Figure 1: Typical DTI volume (taken from Fiber ViewerGoodlett et al, 2005) (A) FA map of the mid-transverse slice of the human head (B) FA map overlaid with the vectormap of the diffusion tensor (C) Zoomed view of the anterior corpus callosum outlined in B showing the 2D vector orientations (D) The 3D axonal tract representation of the corpus callosum and the corona radiata.

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matter tract representations, which can be broadly classified into two types:
deterministic and probabilistic. Techniques classified in the first category are
based on line propagation algorithms that use local tensor information for
each step of the propagation. The main differences among techniques stems
from the way information from neighbouring pixels is incorporated to define
smooth trajectories or to minimize noise contributions. The second type of

<sup>1</sup> approach is based on global energy minimization to find the energetically <sup>2</sup> most favourable path between two predetermined pixels. The most intuitive <sup>3</sup> way to reconstruct a 3D trajectory from a 3D vector field is to propagate a <sup>4</sup> line from a seed point by following the local vector orientation (Figure 1D) <sup>5</sup> where the mean diffusivity is represented by  $\lambda'$  which is generated from the <sup>6</sup> principal eigenvalues ( $\lambda_1, \lambda_2, \lambda_3$ ) by the equation

$$\lambda' = (\lambda_1 + \lambda_2 + \lambda_3)/3 \tag{1}$$

<sup>7</sup> The FA index measures the fraction of the magnitude of the effective diffusion <sup>8</sup> tensor that is ascribed to the anisotropic diffusion. FA is is quantitative and <sup>9</sup> dimensionless. For an isotropic medium, FA = 0 and for a cylindrically <sup>10</sup> symmetric anisotropic medium ( i.e.,  $\lambda_1 > \lambda_2$ ,  $\lambda_2 = \lambda_3$ ), FA =1 (Basser and <sup>11</sup> Pierpaoli, 1996). The anisotropy (FA) of the voxel containing the diffusion <sup>12</sup> tensor is generated by the equation

$$FA = \sqrt{\frac{1}{2}} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}}{\sqrt{((\lambda_1)^2 + (\lambda_2)^2 + (\lambda_3)^2)}}$$
(2)

The linear propagation approach, which was dubbed FACT (fibre assignment 13 by continuous tracking) (Mori et al., 1999), was used to reconstruct the tract 14 trajectories. The vector information contained at each voxel may not fully 15 reflect the propagation of all the neurons within each voxel but instead it 16 reflects the principal orientation of the fibres within each voxel. This is due 17 to the resolution capabilities of the MRI. The average central nervous system 18 axon is approximately  $1\mu m$  in diameter and the voxel size in this study is 19 2x2x2 mm and regions where fibres cross maybe represented as isotropic (eq. 20 2) but may in fact, contain two distinct tensor propagations (Tuch et al., 21 2002). However, the tensor information that is used in the FE model is 22 fitted to the elements with an approximate size of  $10mm^3$  and the distinct 23 tensors that define each voxel region are again averaged to give the gross 24 representation of the fibre orientations of each element in the UCDBTM 25 head model. 26

#### 27 2.1. Mesh morphing to apply orientations

The location and orientation of the tensor information and the FA is mapped to each element by registering the elements that comprise the brain in the 3D FE model to the 3D FA volume of the brain. Registration of DT images requires optimisation of tensor reorientation (Alexander et al, 2001;

Curran and Alexander, 2003, 2004; Zhang et al. 2006). However, the FE 1 elements were mapped to the FA volume negating the requirement for tensor 2 reorientation. Creation of another subject specific FE model of the entire 3 head was considered to be beyond the scope of this present work. Instead 4 the existing validated model was morphed to the 3D MR volume using a 5 thin-plate splines method to compute the full-field transformations between 6 source (FE model) and target (FA volume). This has the basis that a plate with isotropic properties (eg. steel) can be morphed to fit a homologous shape 8 (a shape that can be formed from the original without joining, crossing or q tearing the original shape) by means of applying forces and constraints to 10 bend the plate to the new desired shape. Instead of writing a program to 11 perform this morphing, a combination of Matlab subroutines and ABAQUS 12 software was used instead to reshape the model. A coarse surface grid mesh 13 of the brain FE model was constructed and this was then warped (simple 14 scaling in the X, Y and Z domains) to fit the global x, y and z dimensions 15 of 3D FA Volume (Mendis et al., 1995). 16

Vectors were constructed by using the node points on the coarse grid and 17 matching landmark points based on the shortest distace from the node grid 18 positions to the surface of the FA volume, until every point on the coarse grid 19 had a displacement vector associated with it. A static displacement analysis, 20 using all of these displacement vectors as input, was then carried out on this 21 coarse grid (giving it isotropic properties). Using Matlab the resultant vector 22 plot was transformed into a continuous spatial displacement field. This new 23 continuous displacement field was then applied to the projection mesh model 24 at the dura and a new static displacement analysis was carried out on the 25 entire projection mesh model (again giving all elements identical isotropic 26 properties). This then forced the intracranial shape to move from its original 27 state to match that of the new intracranial shape. Finally the analysis results 28 were used to create an applied spatial transformation in Matlab which moved 29 the original nodal positions, strain free, to those of the deformed positions. 30 This process was used to find the principle orientation of each element in 31 the original FE space; the anisotropy from DTI was then integrated with the 32 model (Figure 2 A and B). 33

#### 34 2.2. Material model

A constitutive model with transversely isotropic hyperelastic mechanical behaviour of a family of collagen fibres for the arterial wall has been developed Gasser et al., (2006) and Holzapfel et al., (2000). Therefore, this model



Figure 2: A 3D eigenvetor representation of the diffusion direction and arbitrary unit direction vector  $\vec{M}$  in terms of Eulerian angles

provides a good bases from which to develop a similar hyperelastic model for 1 anisotropic regions of brain tissue. It is assumed that there is only one family 2 of axonal fibre bundles and these axonal fibres are embedded in an isotropic 3 incompressible matrix. These axonal fibres are distributed uniaxially in an 4 inferior-superior direction. For the purpose of simplification, the preferred 5 fibre direction vector,  $\overrightarrow{n_0}$ , is aligned within a local rectangular cartesian coor-6 dinate system and the orientation density function is independent of Eulerian angle,  $\Phi$ , as defined in the DTI tensor. Therefore, the orientation density function,  $\rho(\vec{M}(\Theta, \Phi))$ , becomes  $\rho(\vec{M}(\Theta))$ . 9

$$\alpha_{11} = \alpha_{22} = k, \alpha_{33} = 1 - 2k, k = \frac{1}{4} \int_0^\pi \rho\left(\vec{M}(\Theta)\right) \sin^3\Theta d\Theta$$
(3)

where the term k has been introduced to represent the fibre distribution and describes the degree of anisotropy. Consequently, the generalized second order structure tensor, H, can be written in compact form.

$$H = kI + (1 - 3k)\vec{n_0}\vec{n_0} \tag{4}$$

where I is the identity tensor. Hence, H depends only on the single dispersion structural parameter k ( $k \in [0, 1/3]$ ).k=0 describes the full alignment of axonal fibres and k = 1/3 describes the isotropic distribution of axonal fibres. The continuum representation of the axonal fibre orientation forms the foundation for an anisotropic hyperelastic formulation. In order to derive the anisotropic hyperelastic strain energy potential W for the brain, it is assumed that it can be separated into an isotropic strain energy potential of the matrix,  $W_m$  and an anisotropic strain energy potential of axonal fibers,  $W_f$ . Therefore, the anisotropic strain energy potential function is

$$W\left(\bar{C}, H_{i}\right) = W_{m}\left(\bar{C}\right) + \sum_{i=1}^{N} W_{fi}\left(\bar{C}, H_{i}(\vec{n_{o}i}, k)\right)$$
(5)

where the general second order structural tensor  $H_i(\overrightarrow{n_{oi}}, k)$  is defined according to equation (4), N is the number of fibre families and  $\overline{C}$  is the isochoric part of the right Cauchy-Green strain tensor C.

The matrix material is modelled as an incompressible isotropic neo-Hookean
model (Ning et al., 2006, Hrapko et al., 2008, Van Dommelen et al., 2008,
Prange and Margulies, 2002), i.e.

$$W_m = C_{10} \left( \overline{I_1} - 3 \right) + \frac{1}{D_1} (J - 1)^2 \tag{6}$$

where  $\overline{I_1}$  denotes the first invariant of  $\overline{C}$ , J is the volume ratio,  $C_{10}$  and  $D_1$  are neo-Hookean coefficients. These neo-Hookean coefficients can be related to the initial shear modulus  $G_0$  and the bulk modulus  $K_0$  as follows

$$C_{10} = \frac{G_0}{2}, D_1 = \frac{2}{K_0} \tag{7}$$

The additional contribution of the anisotropic strain energy potential for the
 *i*th family of axonal fibres is

$$W_{fi}\left(\bar{C}, H_{i}\right) = \frac{k_{1}}{2k_{2}} \sum_{i=1}^{N} \left(e^{k_{2}\bar{E}_{1}^{2}} - 1\right)$$
(8)

where  $k_1 > 0$  is a stress parameter to quantify mechanical tensile strength of the axonal fibres and  $k_2 > 0$  is a dimensionless parameter. The important fundamental hypothesis of the Holzapfel-Gasser-Ogden model (Abaqus, 2007) is that the axonal fibres cannot support any compression and would buckle under compressive load, i.e, fibres contribute only their mechanical strength
during tension. The strain energy potential function of the isotropic matrix
and the contribution from the anisotropic axonal fibre reinforcements is given
by

$$W = C_{10} \left( \bar{I}_1 - 3 \right) + \frac{1}{D_1} \left( \frac{J^2 - 1}{2} - \ln J \right) + \frac{k_1}{2k_2} \sum_{i=1}^N \left( e^{k_2 \langle \bar{E}_i \rangle^2} - 1 \right)$$
(9)

This Holzapfel-Gasser-Ogden material definition was used to model the white matter tracts using the direction dependant material properties in the literature (Arbogast and Margulies, 1999; Prange and Margulies, 2002; Ning et al., 2006), as summarised in Table 1.

Brain	$G_0$	$C_{10}$	$K_0$	$D_1$	$k_1$	$k_2$	k
	[Pa]	[Pa]	[GPa]	[1/GPa]	[Pa]		
Brain	315.17	157.88	2	1	3013.30	0.00001	FA
Brainstem	12.7	6.35	2	1	121.2	01	FA

Table 1: Material properties of the brain

The dispersion parameter k is defined based on the average fractional anisotropy
equation (2) of the fibres for each element group. The material properties
of the brain stem are highly anisotropic in nature and are defined separately
to the remaining brain tissue that constitute the elements of the cerebrum.
The material properties for the remaining parts of the model, i.e., the cortical

and trabecular bone, scalp and intracranial membranes were taken from the
literature (Horgan and Gilchrist, 2003).

The UCDBTM, which is a freely available, validated 3D finite element model of the head, can simulate the effect of the overall head movement on the cranial contents, so the local deformation parameters within the brain tissue can be examined and compared to the observed clinical results. The analysis of the model boundary conditions and mesh sensitivity have been previously assessed (Horgan and Gilchrist, 2003, 2004) while validating the model against linear and rotational impact cadaver tests.

An experimental study of high rotational acceleration/deceleration on monkeys (Gennarelli et al., 1982) reported the conditions required to produce diffuse axonal injury (DAI). At levels of acceleration below 175  $krad/s^2$ 

Material	Young's	Poisson's	Density
	modulus	ratio	(kg/m3)
	(MPA)		
scalp	16.7	0.42	1000
Cortical bone	15000	0.22	2000
Trabecular	1000	0.24	1300
bone			
Dura	31.5	0.45	1130
Pia	11.5	0.45	1130
Falx and Ten-	31.5	0.45	1130
torium			
Facial Bone	5000	0.23	2100

Table 2: Material properties of the remaining head structures

and pulse duration below 5ms cerebral concussion was present and it was 1 proposed that a shear strain of 0.05 was necessary to cause concussion (Mar-2 gulies and Thibault, 1994). This rotational acceleration was applied in the 3 sagittal plane around the centre of mass of the present 3D model with both 4 the anisotropic material properties (i.e., k = 0) and isotropic material prop-5 erties (i.e., k = 1/3) from the literature (Table 1). Elements were segmented 6 manually and grouped together to represent specifc structures and regions based on the segmented fibre bundle representations in the DTI data set. 8 The gross orientations were overlaid onto the FE head model.

## 10 3. Results

The predicted regions affected by axonal injury were based on the shear strain response of each material model and the results of which are presented in Figure 3. The model predicted a statistically significant difference between homogenous and anisotropic material definitions at both the brainstem and the corona radiata (p<0.05) regions. However, within the midbrain, corpus callosum and grey matter regions, no significant difference was predicted by using either isotropic or anisotropic properties.

These two regions where differences were observed are highly anisotropic with a median fractional anisotropy (FA) value of 0.7 with a standard deviation of 0.003. The grey matter however does not have a principle orientation



Figure 3: The mean values and standard deviations observed in the simulations for strain based measures

and has a max FA of less than 0.1. No statistically significant difference 1 was found between the shear strain of the anisotropic grey matter and the 2 homogenous grey matter (p < 0.01). Similarly too, no statistically significant 3 difference in axonal injury was predicted between the material models for the Corpus Callosum and the Midbrain. These regions have FA values of 0.8 and 5 0.7 respectively and are highly anisotropic and a larger variation between 6 the material responses was expected. This may be due to the location of 7 the centre of mass around which the rotation takes place and the principle orientations of the white matter in these regions lie along the axis of rotation. 9 This would result in a reduction in the shear forces acting in these fibres. 10

## 11 4. Discussion

In current research, finite element modelling is the primary tool used to investigate the mechanics of TBI. However the material models are crucial in accurately predicting the circumstances that cause TBI. The approach of

combining in-vivo measurements of the orientations of normal healthy ax-1 onal fibre bundles with FE models could improve the predictive capabilities 2 using FE simulations in DAI. The current practice of using homogenous ma-3 terial properties may lead to erroneous results in the reported values of injury 4 in numerical accident reconstruction. The initial quality of the elements in 5 the present model was assessed and confirmed to be adequate and the to-6 tal energy remained constant while the hourglassing energy was insignificant 7 compared to the total energy in the calculations (<10%). However, one pos-8 sible limitation of the present model is the relatively low mesh density of the 9 head model in comparison to the DTI data. This limits the geometrical de-10 tail that would be required to model each individual axonal tract, especially 11 the interface between grey and white matter tracts and the boundaries of 12 the ventricular system and white matter. Another limitation of the model is 13 the orientation of the tensors within each element. The registration method 14 may not fully map each voxel to its exact location within each element and 15 the method of generating the tracts could also lead to errors in the ellipsoid 16 placement. However subject specific models with a mesh density of  $1mm^3$ 17 along with higher order tensor data and noise reduction methods would im-18 prove the FE predictions but would also increase the computation time of 19 each simulation. 20

## 21 5. Conclusion

The FE model predictions illustrate the importance of the orientation of the material structure in diffuse axonal injury. The anisotropic model predicted a greater level of injury at sites distal to the centre of rotation than a simple isotropic model. These findings illustrate that the anisotropic model shows a varation in the predicted apoptosis at sites distal to the centre of rotation in diffuse axonal injury simulation. ABAQUS, version 6.9-2, (2007) ABAQUS analysis: user's manual, Dassault
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